

What is claimed is:

1. A microparticle less than about 100 microns in diameter, comprising:  
a polymeric matrix;  
5 a lipid having a pKa of less than about 2.5; and  
a nucleic acid molecule, wherein the microparticle is not encapsulated in a  
liposome and the microparticle does not comprise a cell.
- 10 2. The microparticle of claim 1, wherein the lipid is selected from the group  
consisting of a lipid sulfonate, lipid sulfate, lipid phosphonate, and lipid phosphate.
- 15 3. The microparticle of claim 1, wherein the lipid is selected from the group  
consisting of polyethylene glycol diacyl ethanolamine, taurocholic acid, glycocholic acid,  
cholic acid, N-lauroyl sarcosine, and phosphatidyl inositol.
- 20 4. The microparticle of claim 1, wherein the lipid is polyethylene glycol  
diacyl ethanolamine.
5. The microparticle of claim 1, wherein the lipid is taurocholic acid.
- 25 6. The microparticle of claim 1, wherein the lipid has a pKa of less than about  
2.0.
7. The microparticle of claim 1, wherein the lipid has a pKa of about 1.8.
8. The microparticle of claim 1, wherein the microparticle has a diameter of  
about 50 microns.

9. The microparticle of claim 1, wherein the nucleic acid molecule is circular.

5      10. The microparticle of claim 1, wherein the nucleic acid molecule is a  
plasmid.

11. The microparticle of claim 1, wherein the nucleic acid molecule  
comprises an expression control sequence operatively linked to a coding sequence.

10      12. The microparticle of claim 1, further comprising a targeting molecule.

13. The microparticle of claim 1, further comprising a stabilizer.

15      14. A preparation of microparticles comprising a plurality of the  
microparticles of claim 1.

15. The microparticle of claim 1, wherein the microparticle does not comprise  
a virus.

20      16. The microparticle of claim 10, wherein the plasmid is at least 50%  
supercoiled.

25      17. A microparticle less than about 100 microns in diameter, comprising:  
a polymeric matrix;  
a zwitterionic lipid; and  
a nucleic acid molecule, wherein the microparticle is not encapsulated in a  
liposome and the microparticle does not comprise a cell.

18. The microparticle of claim 17, wherein the lipid is selected from the group consisting of CHAPSO (3-3-(Cholamidopropyl)dimethylammonio]-2-hydroxy-1-propanesulfonate), CHAPS ((3-3-(Cholamidopropyl)dimethylammonio]- 1-propanesulfonate, and phosphatidylethanolamine.

19. The microparticle of claim 17, wherein the microparticle does not comprise a virus.

20. The microparticle of claim 17, wherein the microparticle has a diameter of about 50 microns.

21. A microparticle less than about 100 microns in diameter, comprising:  
a polymeric matrix;  
a lipid having a pKa of less than about 2.5; and  
a nucleic acid molecule comprising an expression control sequence operatively linked to a coding sequence, wherein the coding sequence encodes an expression product selected from the group consisting of:

(a) a polypeptide at least 7 amino acids in length, having a sequence essentially identical to the sequence of (i) a fragment of a naturally-occurring mammalian protein; or (ii) a fragment of a naturally-occurring protein from an infectious agent that infects a mammal; or (iii) a plurality of the fragments of (i), linked in tandem; or (iv) a plurality of the fragments of (ii), linked in tandem;

(b) a peptide having a length and sequence that permit it to bind to an MHC class I or II molecule;

(c) a polypeptide consisting of at least two peptides of (b) either linked in tandem or sharing an overlapping sequence; and

(d) any of (a), (b), or (c) linked to a trafficking sequence,  
provided that the expression product optionally includes an amino terminal  
methionine residue, and further provided that the expression product does not have an  
amino acid sequence identical to that of a full-length, naturally-occurring protein.

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22. The microparticle of claim 21, wherein the expression product is a  
polypeptide consisting of at least two peptides of (b) linked in tandem, wherein the at  
least two peptides of (b) are not identical.

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23. The microparticle of claim 21, wherein the expression product is a  
polypeptide consisting of at least two overlapping peptides of (b).

24. The microparticle of claim 21, wherein the expression product comprises  
a peptide having a length and sequence that permit it to bind an MHC class I molecule.

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25. The microparticle of claim 21, wherein the expression product comprises  
a peptide having a length and sequence that permit it to bind an MHC class II molecule.

26. The microparticle of claim 21, wherein the expression product is  
immunogenic.

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27. A preparation of microparticles comprising the microparticle of claim 21.

28. The microparticle of claim 21, wherein the microparticle has a diameter  
of about 50 microns.

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29. A method of administering a nucleic acid to an animal, comprising

providing the microparticle of claim 1; and  
introducing the microparticle into the animal.

30. A method of administering a nucleic acid to an animal, comprising  
providing the microparticle of claim 17; and  
introducing the microparticle into the animal.

31. A method of administering a nucleic acid to an animal, comprising  
providing the microparticle of claim 21; and  
introducing the microparticle into the animal.

32. The method of claim 29, wherein the microparticle is introduced into a  
mucosal tissue of the animal.

33. The method of claim 29, wherein the mucosal tissue is vaginal tissue.

34. The method of claim 29, wherein the mucosal tissue is rectal tissue.

35. A process for preparing microparticles, comprising:

- (1) providing a first solution comprising a polymer and a lipid having a pKa  
of less than about 2.5;
- (2) providing a second solution comprising a nucleic acid dissolved or  
suspended in a solvent;
- (3) mixing the first and second solutions to form a first emulsion; and
- (4) mixing the first emulsion with a third solution to form a second emulsion;

wherein both mixing steps are carried out in a manner that minimizes shearing of the nucleic acid while producing microparticles having an average diameter smaller than 100 microns.

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36. The process of claim 35, further comprising:

(5) washing the microparticles with an aqueous solution to remove the solvent;

(6) concentrating the microparticles; and

(7) lyophilizing the microparticles.

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